LINDANE

GENERAL INFORMATION

Lindane belongs to the organochlorine (OC) pesticide class. This is one of the oldest classes of pesticides, and few OCs are still in use today. OC pesticides are so named because they include carbon, hydrogen, and chlorine. There are three major subclasses of OC pesticides: diphenyl aliphatics, cyclodienes, and hexachlorocyclohexane (HCH). The well-known pesticide DDT belongs to the first class. The HCH subclass is not so much a class as the collection of the five isomers of HCH: alpha (α), beta (β), gamma (γ), delta (δ), and epsilon (ϵ). Only the gamma isomer has insecticidal properties. This is the isomer manufactured as lindane.[1] Lindane has not been produced in the United States since 1977, but it is imported in multiple forms for pharmacologic and industrial use. The use of lindane is restricted by the EPA; it can be applied only by certified pesticide applicators.

Lindane production involves the purification of technical grade HCH (16 percent α-HCH, 7 percent β-HCH, 45 percent γ-HCH) to a 99.8 percent pure product. The α-HCH and β-HCH isomers (which have a half-life of seven to eight years) are metabolized, but γ-HCH is metabolized much faster (its half-life is less than one day); therefore, most metabolites recovered in urine are from the gamma isomer (i.e., lindane). The most common human metabolites observed are 2,3,5-trichlorophenol, 2,4,5-trichlorophenol, 2,4,6-trichlorophenol, and 2,4-dichlorophenol (Angerer et al., 1983).

Lindane has been used to control a wide variety of insect pests in agricultural, public health, and medicinal applications. It is available as a suspension, emulsifiable concentrate, fumigant, seed treatment, wettable and dustable powder,

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[1] This report focuses on exposure to lindane because this is the compound to which PGWV may have been exposed.

and ultra-low-volume (ULV) liquid. The chemical identity of lindane is shown
in Table 4.1, and Table 4.2 summarizes its physical and chemical properties.

Table 4.1

Chemical Identity of Lindane

Characteristic	Information
Chemical class	Organochlorine
Chemical name[a]	γ-1,2,3,4,5,6-hexachlorocyclohexane
Trade names	Agrocide, Ambrocide, Aparasin, Aphatiria, Benesan, Benexane, BoreKil, BorerTox, Exagama, Gallogama, Gamaphex, Gammalin, Gamma-Col, Gamene, Gamiso, Gammex, Gammexane, Gamasan, Gexane, Isotox, Jacutin, Kwell, Lindafor, Lindaterra, Lindatox, Lorexane, New Kotol, Noviagam, Quellada, Steward, Streunex, Tri-6, Viton
Chemical formula	$C_6H_6Cl_6$
CAS Registry number	58-89-9

[a]Lindane (HCH) has historically and widely been inappropriately referred to as benzene hexa-
chloride (BHC). This compound should not be confused with hexachlorobenzene (HCB) (Kamrin,
1997).

Table 4.2

Physical and Chemical Properties of Lindane

Property	Information
Molecular weight	290.85
Color/form	Colorless to white crystalline powder/solid
Odor	Odorless to slight musty or aromatic odor
Water solubility at 25°C	Insoluble
Partition coefficient (K_{ow})	5,248
Soil sorption coefficient (K_{oc})	1,100
Vapor pressure at 20°C	9.4×10^{-6} mm Hg
EPA toxicity classification	Class II
ACGIH TLV–TWA	0.5 mg/m^3 (skin)
NIOSH REL–TWA	0.5 mg/m^3 (skin)
NIOSH REL–STEL	NA
NIOSH IDLH value	50 mg/m^3
OSHA PEL–TWA	0.5 mg/m^3 (skin)
EPA IRIS RfD	3×10^{-4} mg/kg/day
EPA IRIS RfC	NA
Carcinogenicity classification	
ACGIH	A3
EPA	NA
IARC	2B

NA = not available.

AVAILABILITY AND RECOMMENDED USE OF LINDANE DURING ODS/DS

Lindane dust was recommended for use during ODS/DS exclusively as a de-lousing agent, so the primary route of potential exposure in veterans was dermal; the secondary route was inhalation. Two lindane products were shipped to the Gulf; these are detailed in Table 4.3.

POTENTIAL HEALTH EFFECTS OF LINDANE

Lindane Metabolism/Pharmacokinetics

The effects of lindane are primarily neurotoxic and are similar to those of DDT, but lindane generally produces a more rapid response, especially in increasing insect respiration to lethal levels, for which it was designed. As with most OC pesticides, lindane interferes with fluxes of cations across nerve cell membranes, increasing neuronal irritability and producing convulsions. These convulsions may result in death by interfering with pulmonary gas exchange and by generating severe metabolic acidosis (Cheremisinoff and King, 1994).

Neurologic effects of lindane exposure have been attributed to alteration of sodium conduction in nerve axons (MacPhail et al., 1999) and on the picrotoxin binding site of the GABA-A receptor complex in the central nervous system (CNS) (Artigas et al., 1988; Suanol et al., 1988). This GABA-A-antagonist property impairs the inhibitory tone GABA exerts on CNS neurons (Artigas et al., 1988; Suanol et al., 1988).

Lindane and its metabolites can be detected and measured in blood and body fluids by clinical laboratory tests. But although lindane can be quantified, it is difficult to derive with certainty specific exposure levels based on measured blood and tissue levels. Further, although lindane metabolites are measurable,

Table 4.3

Formulations of Lindane Available During ODS/DS

National Stock Number (NSN)	Name	Form	Formu-lation (%)	Unit Size	Application Directions
6840-00-242-4217	Lindane	Dust	1	2-oz can	Treat clothing; emergency use only
6840-00-242-4219	MIL-I-11490E	Dust	1	25-lb can	Treat clothing; emergency use only

Source: Provided by OSAGWI.

other environmental compounds, particularly chlorobenzene, produce the same metabolites.

Lindane has been widely used for about 50 years as an insecticide on crops and in medicinal formulas to treat head lice and scabies, so there exists a fair amount of data on its efficacy, safety, and toxicity (Parent-Massin et al., 1994). The primary routes of exposure are dermal absorption, ingestion, and inhalation.

Acute Effects

Dermal Exposure. Dermal exposure is an important consideration when evaluating lindane toxicity because of lindane's therapeutic use as a scabicide in creams and lotions and its use as a delousing agent during the Gulf War. Lindane is efficiently absorbed through human skin (Feldman and Maibach, 1974; Ginsburg et al., 1977). Hosler et al. observed a rise in plasma lindane from nondetectable levels to 10.3 ng/mL three days after dermal application of a 1 percent solution (Hosler et al., 1980).

Studies by Dick et al. demonstrated differential absorption depending on the vehicle (solvent) in which lindane is dissolved (Dick et al., 1997a,b). When an acetone formulation was used, the peak absorption period varied from three to 45 hours in volunteers; however, when white spirit (a commercial wood preservative) was used, the peak occurred more reliably, at 6.5 ±1.6 hours, and absorption was about twentyfold greater (Dick et al., 1997a). Animal studies confirm that ^{14}C radiolabeled lindane in acetone is effectively absorbed, with 18 percent, 34 percent, and 54 percent absorption of a dose applied topically to the forearm, forehead, and palm of rhesus monkeys (Moody and Ritter, 1989). A similar evaluation in rats showed 31 percent absorption following mid-dorsal application.

Animal studies substantiate the acute effects of lindane following dermal exposure. Rabbits given a single application of 1 percent lindane (total = 60 mg/kg) exhibited hyperexcitability, seizures, and convulsions (Hanig et al., 1976). Younger animals were more sensitive to the compound than their older counterparts. Ullmann (1986a) reported sedation for 24 hours in rats with a single applied dose of 1 g/kg. Repeated application of lindane to rats (0.18 mg lindane/kg 15 times over 25 days) produced a mild dermatitis (Dikshith et al., 1973), although a single application of 132 mg/kg to rabbits for four hours failed to produce toxicity (Ullmann, 1986c). Blood levels exceeding 20 ng/mL have been associated with neurologic effects (Czegledi-Janko and Avar, 1970; Dick et al., 1997a).

Death has been well documented in animals exposed to high doses of lindane. The LD_{50} for dermal exposure[2] in rats appears to be approximately 500 to 1,000 mg/kg (Gaines, 1960; Ullman, 1986a). In an accident, 10 grams of lindane were sprayed on each of 30 Charolais calves (300 kg) (Venant and Sery, 1991). The calves quickly showed muscular twitching, incoordination, and salivation. Two died one day after exposure, two died the following week, and a fifth died at five months. At 17 days, blood lindane in the surviving calves was measured at 130 ng/mL, dropping 70 percent between day 17 and day 56.

The literature contains several reports (most of them single cases) of human toxicity following dermal application of lindane, generally because of misapplication of a 1 percent solution. Illustrative cases are described in Table 4.4.

In 1996, the U.S. Food and Drug Administration (FDA) required manufacturers of lindane for pharmacologic use to caution consumers about the potential adverse consequences of misuse. The FDA acknowledged that the compound is safe and effective when appropriately used, but lindane treatments are often misused for several reasons. First, because dermal irritation persists for some period following parasite elimination, patients (and parents, in the case of children) may confuse continued pruritis with continued or repeated infestation. Some may also overtreat in an attempt to expedite symptom resolution. In general, the FDA recommends that other treatments be used except in patients who have failed those treatments or who are unable to tolerate them.

Oral Exposure. The clearest evidence of lindane toxicity comes from experimental and observational studies following oral exposure. Animal studies show neurologic and reproductive effects following acute exposure (Table 4.5). Young rats fed subconvulsant levels of lindane following birth exhibited clear behavioral changes (Rivera et al., 1998). Lindane readily crosses the placenta of Wistar rats, with concentrations being particularly high when exposure occurs later in gestation as fetal fat content increases (Khanna et al., 1991).

The literature contains a number of cases of accidental human lindane ingestion, primarily by adults who did not understand the method of treatment or by infants; there are also cases of individuals ingesting lindane intentionally. The most common acute manifestations include neurologic findings, particularly seizure, in addition to tremor, depressed mental status, vomiting, and coma. The first case shown in Table 4.6 was a 43-year-old female who intentionally ingested eight ounces of a 20 percent lindane solution. She developed a diffuse intravascular coagulopathy (DIC) that improved as serum lindane levels de-

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[2]LD_{50} is the median lethal dose. This is a statistically derived single dose that can be expected to cause death in 50 percent of test animals when administered by the route indicated. It is expressed as the weight of a substance per unit weight of animal.

Table 4.4

Reports of Acute Lindane Toxicity in Humans Following Dermal Application

Reference	Age of Subject	How Applied	Blood Level	Manifestations
Boffa et al., 1995	18 yr	Three consecutive daily treatments	50 ng/mL at 2 days, 10 ng/mL at 4 days	Dermatitis and drowsiness at second application, grand mal seizure after third application. Condition resolved without residual findings.
Davies et al., 1983	2 mo (child born premature)	To abdomen and legs for 2 days, then entire body, left on for 18 hours	33 ng/mL	Death. This is the only case of death found from a dermal application of lindane.
Fischer, 1994	24 yr	Two treatments over 1 hour (1.5 times recommended dose) to excoriated skin areas	3 ng/mL 20 hr following the exposure	Visual hallucinations, involuntary movements. Returned to baseline 48 hours following symptom onset.
Pramanik and Hansen, 1979	Premature infant	Not stated	17 times greater than expected following a single dose	Seizures and abnormal neurologic findings.
Telch and Jarvis, 1982	18 mo	Two consecutive nights after hot bath	450, 80, and 29 ppb at 12, 24, and 96 hr, respectively	Seizure lasting 30 minutes 12 hours following second application. Disoriented, lethargic and restless, with tonic-clonic movements. Recovered.
Derek, 1984	23 yr	Applied to entire body one time, second application 1 wk later	Not reported	Tired, weak, and dizzy with imbalance and slurred speech at 12 hours after first application, clearing 12 hours later. After second application, loss of consciousness three times. Recovered after 24 hours.
Shuster, 1996	9 yr	Applied 3 times over 6 days, left on 10–15 min	Not reported	Severe headache, confusion. Recovered completely at 3 days.

Table 4.5

Reports of Acute Lindane Toxicity in Animals Following Oral Exposure

Reference	Animal Model	Concentration and Duration	Effect
Tilsonet al., 1987	Fischer-344 rats	15 mg/kg; or 30 mg/kg	Behavioral: decreased avoidance responses early; impaired passive avoidance retention at 7 days with 30 mg/kg dose.
Rivera et al., 1998	Wistar rats, immature	20 mg/kg single dose; or 10 mg/kg for 7 days	Behavioral: passive avoidance behavior improved with both dosings. The single dose decreased motor activity; the 7 day dosing increased motor activity.
Llorens et al., 1989	Wistar rats	10 mg/kg; 20 mg/kg or 30 mg/kg	Neuromuscular: decreased spontaneous behavior following exposure. Minimally effective dose determined to be 1.85 mg/kg.
Saxena et al., 1986	ITRC-bred albino rats (female)	20 mg/kg; gestation days 6 through 14	Reproductive: no significant fetal abnormalities with lindane alone. When lindane was combined with cadmium, there was significant decrease in body weight, increased embryonic deaths, and increased skeletal deformities.
Dalsenter et al., 1996	Wistar rats (male)	6 mg/kg for 5 days; or 30 mg/kg single dose	Reproductive: reduced spermatid and spermatozoa with histologic evidence of seminiferous tubule damage. Testicular toxicity not accompanied by overt evidence of toxicity.
Sircar and Lahiri, 1989	Swiss mice (female)		Reproductive: hormone deficiency (correctable with estrogen/progesterone) leading to reproductive and developmental failure.
Camaon et al., 1988	Rats	30 mg/kg single dose; or 10 mg/kg for 7 days	Metabolic: single dose induced hypothermia, particularly in the setting of cold stress (approximately –0.5°C). The lower, longer dose did not have this effect.

Table 4.6

Reports of Acute Lindane Toxicity in Humans Following Oral Exposure

Reference	Age of Subject	Blood Level	Time Since Ingestion	Manifestations
Sunder et al., 1988	43 yr	1.3 µg/mL	12 hr	Seizure, rhabdomyolysis, diffuse intravascular coagulopathy, death.
Starr and Clifford, 1972	2.5 yr	0.84 µg/mL	2 hr	Seizure.
Davies et al., 1983	16 yr	0.206 µg/mL	Approx. 2 hr	Seizure, coma. Regained function.
Munk and Nantel, 1977	35 yr	0.6 µg/mL	NA	Seizure, myonecrosis, pancreatitis.
Daerr et al., 1985	16 yr	0.25 µg/mL	Unknown	Lethargy, resting tremor.
Dale et al., 1966	NA	0.29 µg/mL	6 hr	Seizure.
Kurt et al., 1986	41 yr	1.3 µg/mL	First day	Death.
Burton et al., 1991	32 yr	0.13 µg/mL	< 2 hr	Vomiting, seizure (pt on phenytoin).
Aks et al., 1995	13 mo	0.32 µg/mL 0.02 µg/mL	4 hr 20 hr	Generalized tonic-clonic seizure. Improved over next few days.
Aks et al., 1995	2 yr	0.26 µg/mL 0.02 µg/mL	18 hr 39.5 hr	Vomiting, petit mal seizure. Improved.
Aks et al., 1995	16 mo	0.012 µg/mL 0.003 µg/mL 0.002 µg/mL	3 hr 7.5 hr 21 hr	Drowsiness.

creased. Despite the improvement in her coagulation profile, she died 11 days following ingestion.

On the basis of limited clinical data, Aks et al. (1995) concluded that lindane follows a two-phase pattern, with the first (distribution) phase having a short, two- to three-hour half-life and the second (elimination) having a longer, 35-hour half-life (range = 11 to 83 hours). Most individuals with acute oral exposures to lindane suffer the types of effects shown in Table 4.6. However, within a short period of time following metabolism of lindane (hours to days), their function returns to baseline without identified residual impairment.

Inhalation and Environmental Exposure. Few studies focus on acute effects of aerosol or environmental exposure of animals to lindane. Ullmann (1986b) exposed Wistar rats to lindane aerosol for four hours, then observed them for the

following three weeks. The study estimated that the LC_{50} was 1,560 mg/m^3.[3] In a subsequent study, exposing CD-1 mice to 10 mg/m^3 five days per week for six hours per day resulted in 16 percent mortality one week after exposure (Klonne and Kintigh, 1988).

Acute human exposure has resulted from accidents either in the manufacture of lindane or in its application in agricultural settings. Acute symptoms in humans exposed to lindane include headache, nausea, vomiting, restlessness, ataxia, tremor, and excitability (Solomon et al., 1977; Brassow et al., 1981). Seizure has been reported with more extensive exposures, although specific levels at the time of exposure are not available. (Czegledi-Janko and Avar, 1970; Mayersdorf and Israeli, 1974)

Chronic, Reproductive, Genetic, and Carcinogenic Effects

Dermal Exposure. Few studies specifically evaluate the effects of chronic dermal exposure to lindane, because the intended use of lindane for treating parasitic infection generally requires only a single application. However, in one study, female rats (Crl:(WI)BR) exposed to 10 mg/kg/day of lindane for 13 weeks (five days per week, six hours per day) exhibited hyperactivity, and those exposed to 60 mg/kg/day demonstrated ataxia and tremors (Brown, 1988). In the same study, mild renal impairment was observed, particularly in male rats exposed to 10 mg/kg/day.

A few studies document human hematologic manifestations, including bone marrow hypoplasia and aplastic anemia, following prolonged dermal exposures to lindane (Woodliff et al., 1966; Vodopick, 1975; Rauch et al., 1990). In vitro studies suggest that hematopoietic precursors, specifically Colony Forming Unit–Granulocyte and Macrophage (CFU–GM), are sensitive to lindane, and human precursors are more sensitive than those of the rat (Parent-Massin et al., 1994).

Oral Exposure. A number of animal studies provide insight into the potential effects of intermediate and chronic oral exposure to lindane (Table 4.7). Most studies focus on the neurologic and reproductive effects following such exposure.

We did not find definitive studies addressing chronic oral exposure to lindane in humans. Although such exposure could result, for example, from consump-

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[3]LC_{50} is the median lethal concentration. This is a statistically derived concentration of a substance that can be expected to cause death in 50 percent of test animals. It is usually expressed as the weight of a substance per weight or volume of water, air, or feed.

Table 4.7

Reports of Chronic Lindane Toxicity in Animals Following Oral Exposure

Reference	Animal Model	Concentration and Duration	Effect
Banerjee et al., 1996	Hissar albino mice	10 ppm, 30 ppm, or 50 ppm for 12 wk	Immunologic: decreased primary humoral immune response at 12 wk for those exposed to the 50-ppm concentration; decreased secondary immune response starting at 3 wk for those exposed to 50 ppm, after 12 wk for those given 30 ppm. No overt signs of toxicity were observed.
Beard et al., 1997	Mink (female)	1 mg/kg/day for 3 wk before breeding, then followed for 8 wk (to weaning)	Reproductive: decreased acceptance of mating after 1 wk (decreased estradiol, reduced sexual receptivity). Whelping rate decreased but number of implantation sites was not impacted. Lindane increased embryo mortality (post-implantation loss), frequently due to loss of complete litters. No overt toxicity exhibited.
Chakravarty et al., 1986	Ducks (female)	20 mg/kg daily for 8 wk; or 20 mg/kg 3 times/wk for 8 wk; or 20 mg/kg 2 times/wk for 8 wk; or 20 mg/kg daily for 8 wk followed by stilbesterol; or 20 mg/kg 3 times/wk for 8 wk followed by stilbesterol	Reproductive: cessation of egg-laying for a period of time, followed by decreased egg-laying. Histology showed undifferentiated follicles but absence of mature vitellogenic and post-ovulatory follicles. Stilbesterol led to resumed egg-laying. Lindane reduced estradiol, reducing yolk protein synthesis.
Lahiri and Chakraborty, 1991	Ducks (female)	20 mg/kg daily for 8 wk; or 20 mg/kg 3 times/wk for 8 wk; or 20 mg/kg twice weekly for 8 wk	Reproductive: decreased serum calcium and calcium in the shell gland, particularly at higher doses. Shell thinning stemming from decreased shell formation and decreased mineral.
Arisi et al., 1994	Wistar rats (male)	1,000 ppm for 90 days	Neurologic: tonic convulsions.
Gilbert, 1995	Long-Evans rats (male)	10 mg/kg for 30 days; or 10 mg/kg 3 times/wk for 10 wk	Neurologic: increased behavioral sensitivity over time, persisting for 4 wk without additional dosing. Accelerated electrical kindling (development of behavioral seizures with repeat initially subthreshold stimuli). These findings were not accompanied by overt toxicity.
Llorens et al., 1992	Wistar rats (male)	10 mg/kg, 6 days/wk, for a total of 25 doses	Neurologic: increased spontaneous motor activity (about 30%) but no other changes (e.g., activity counts over 23 hr) 2 wk after exposure.
Wolff et al., 1987	F-1 hybrid mice (female)	160 ppm for 6, 12, 18, or 24 months	Neoplastic: different phenotypes showed different prevalence for clara cell hyperplasia and various (e.g., lung, liver) adenomas, and hepatocellular carcinoma.
Rivett et al., 1978	Beagle dogs	25, 50, or 100 ppm for 2 years; or 200 ppm for 32 weeks	Neurologic: minor EEG changes were observed with the 200-ppm exposure. GI: liver color appeared darker with the 100- and 200-ppm exposures but not with the 50-ppm exposure. No other adverse effects were observed.

tion of low levels of the pesticide in contaminated food products or from breast feeding (Ladodo et al., 1997; Al-Saleh et al., 1998), reported cases of lindane ingestion focus on acute accidental or intentional ingestion.

Inhalation and Environmental Exposure.   There are few animal studies of chronic aerosol, vapor, or environmental lindane exposure. One study of CD-1 mice exposed to a lindane dust aerosol six hours per day, five days per week, reported a 22 percent mortality rate with exposure of 5 mg/m^3 for up to 20 weeks and a 2 percent mortality rate when the exposure was reduced to 1 mg/m^3 (Klonne and Kintigh, 1988).

Several reports discuss human exposure to lindane as an environmental toxicant. Lindane has been used in vaporizers and included among other chemicals in wood preservatives, as well as in agricultural settings. Individuals employed in the manufacture of lindane are also exposed; however, as discussed previously, these individuals are exposed to a combination of HCH isomers with different effects in biological systems (Baumann et al., 1980; Angerer et al., 1983). Some situations have precipitated unintentional prolonged exposures to low levels of lindane in the environment. Reports in the literature are either anecdotal or of an epidemiologic case-control nature, where subjects may have been exposed to a number of chemical toxicants simultaneously, making it difficult to attribute specific effects to individual chemical exposures.

Brassow et al. compared the health status, including laboratory parameters, of 60 German males employed in a plant producing lindane to that of 20 male clerks not so exposed (Brassow et al., 1981). The exposed individuals exhibited some statistical differences in laboratory parameters (i.e., increased neutrophil percent, decreased lymphocyte percent, increased reticulocyte counts, longer prothrombin times, and decreased serum creatinine and uric acid). Other laboratory variables, including total white cell count, standard urinalysis analytes (i.e., protein, glucose, urobilinogen), and liver enzymes, were not statistically different between the groups. No overt signs of toxicity were observed.

Cantor et al. studied agricultural exposure to 23 insecticides used on animals, 34 insecticides used on crops, 38 herbicides, and 16 fungicides, comparing exposed and non-exposed individuals to assess the risk of non-Hodgkin's lymphoma (Cantor et al., 1992). Table 4.8 summarizes their observations.

These findings suggest an increased lymphoma risk among farmers exposed before 1965 or not using protective clothing or equipment. Another case-control study of midwestern Caucasian men showed a similar association (Blair et al., 1998). However, it is again difficult to interpret individual pesticide risks because of multiple exposures, and because so many substances were studied simultaneously, the chance of spurious association with some is increased.

Table 4.8

Comparison of Exposures to Agricultural Chemicals Resulting in Risk of Non-Hodgkin's Lymphoma

	Ever Handled		Handled Before 1965	
Application	Odds Ratio	Confidence Interval	Odds Ratio	Confidence Interval
Lindane used as an animal insecticide	1.4	1.0–2.1	1.7	1.1–2.7
Lindane used as a crop insecticide	2.0	1.0–3.7	2.2	1.0–4.7
With use of protective equipment	2.0	1.0–3.7	—	—
Without use of protective equipment	—	—	2.6	1.2–5.5

In a limited study of 22 patients meeting the CDC definition of chronic fatigue syndrome (CFS) (Holmes et al., 1988), 17 patients with CFS symptoms but with a toxic exposure excluding them from the strict definition of CFS, and 34 control subjects, lindane was not detected in subjects (Dunstan et al., 1995). However, the incidence of other OC contamination (e.g., hexachlorobenzene) was statistically more likely to be present in those with CFS.

Several studies in the literature address the impact of environmental exposure to toxic substances, including lindane, on human reproduction (Saxena et al., 1980; Karmaus and Wolf, 1995; Gerhard et al., 1998). A German study assessed reproductive outcomes among female teachers exposed to wood preservatives in a daycare center (Karmaus and Wolf, 1995). Pregnancies in exposed women ended more frequently in induced or spontaneous abortions or in caesarian sections. Live births had reduced birth weights and infant body lengths comparable to those of infants whose mothers were not exposed; however, the study could not control for paternal factors. In addition to lindane, these teachers were exposed to pentachlorophenol (PCP) and trace amounts of other chemicals formed during the preservative production process. Saxena et al. also observed an association between OC levels in blood and placental tissue and premature labor and abortion (Saxena et al., 1980).

An Israeli study detected a statistically significant correlation between OC and polychlorinated biphenyl concentrations and the presence of oligospermia, defined as sperm counts below 20 million/mL (Pines et al., 1987). The control group (fertile males) had a mean lindane level of 1.13 ng/g serum (median 0.9 ng/g), whereas infertile males had a mean lindane level of 2.28 ng/g (median = 1.15 ng/g).

Another study examined the psychological impact of chronic exposure to wood-preserving chemicals known to contain lindane and PCP (Peper et al., 1999). Fifteen German women identified from a large number of individuals seeking care at a women's health center had been exposed to these chemicals

for at least five years (mean = 10 years). There were statistically significant differences in blood lindane and PCP levels of exposed women compared with those of unexposed controls. Using a series of psychological profile instruments, the investigators also found statistical differences in subjective complaints (i.e., attenuated motivation, fatigue, distractibility, and depressed mood) and memory parameters (e.g., verbal memory span, working memory, visual short-term retention, verbal fluency) among the individuals with pesticide exposure.

SYNTHESIS

Lindane is a well-known and extensively studied pesticide that is generally considered safe when used as directed.

Acute exposure precipitates neurologic changes including hyperexcitability, tremor, and coma. Many of these abnormalities are reversible with supportive care. However, deaths have been reported following lindane ingestion. In two of these cases, the victims had blood levels exceeding 1 µg/mL.

Epidemiologic studies in the literature suggest the possibility of subtle long-term neurologic and reproductive health effects; however, subjects in these studies were exposed to a number of different potentially toxic substances, making it difficult to attribute findings specifically to lindane.

Because of the potential risks associated with lindane, its use is no longer recommended as the first-line drug therapy for treating scabies and body lice. Although individuals should use lindane with caution, when used appropriately, it is generally considered a safe and effective pesticide.